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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,728	07/21/2006	Bertram Jacobs	01231.0023U2	1957
23859 7590 07/06/2007 NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915			EXAMINER WHITEMAN, BRIAN A	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 07/06/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/563,728	Applicant(s) JACOBS ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2007.
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-10 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 06 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/8/06, 1/8/06</u> | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1-10 are pending.

Election/Restrictions

Applicant's election of Group I (claims 1-10) and species E3L in claim 4 in the reply filed on 5/2/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

KSL and combination thereof in claim 4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/2/07.

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C.120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant

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application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the

petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required.

Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

The examiner has considered the international search report.

The references cited in the Search Report 1/6/06 have been considered, and will be listed on any patent resulting from this application because they were provided on a separate list in compliance with 37 CFR 1.98(a)(1).

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 1 and 3-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Roberts et al. (A2, cited on an IDS). Roberts et al. teach a method of treating neoplasm in a mammal using a vaccinia virus having a mutation in the E3L gene (pages 10 and 26). Roberts et al. teach the neoplasm can be breast or prostate (page 11). The skilled artisan can administer the virus using intravenous administration (page 11). With respect to the limitation "reduced ability to inhibit PKR and increased sensitivity to interferon" in instant claim 8 the vaccinia virus taught in the prior art reads on the product recited in claim 8. Thus, a product with the same structural as another product should have the same properties as that product.

A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

MPEP 2112.01:

PRODUCT AND APPARATUS CLAIMS □ WHEN THE STRUCTURE RECITED IN THE REFERENCE IS SUBSTANTIALLY IDENTICAL TO THAT OF THE CLAIMS, CLAIMED PROPERTIES OR FUNCTIONS ARE PRESUMED TO BE INHERENT

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Claims 1 and 4-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (Virology 199, 491-496, 1994). Lee et al. teach apoptosis in a cancer cell line (HeLa) exposed to vaccinia virus lacking an E3l gene (abstract). With respect to the limitation "reduced ability to inhibit PKR and increased sensitivity to interferon" in instant claim 8 the vaccinia virus taught in the prior art reads on the product recited in claim 8. See *In re Best* and *In re Spada*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (A2, cited on an IDS) taken with Coffey et al. (US 20020028195). Roberts et al. teach a method of treating neoplasm in a mammal using a vaccinia virus having a mutation in the E3L gene (pages 10 and 26). Roberts et al. teach the neoplasm can be breast or prostate (page 11). However, Roberts et al. does not specifically teach administering the virus to cancer cells that are ras-transformed cells.

However, at the time the invention was made, Coffey teaches administering modified vaccinia virus to ras-transformed cells (page 2). "Mutation or deletion of the genes responsible for antagonizing PKR should prevent viral replication in cells in which the PKR activity is normal (i.e. normal cells) (page 2)." "However, if infected cells are unable to activate the antiviral response mediated through PKR (i.e., Ras-mediated tumor cells), then these mutant viruses should replicate unheeded and cause cell death (page 2)." "Therefore, these mutant viruses can replicate preferentially in Ras-transformed cells where it is determined that PKR is unable to function (page 2)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roberts et al. taken with Coffey, namely to administer modified vaccinia virus to ras-transformed cells. One of ordinary skill in the art would have been motivated to combine the teaching since viruses can replicate preferentially in ras-transformed cells where PKR is unable to function.

In view of Roberts and Coffey, one of ordinary skill in the art would have had a reasonable expectation of success for administering the virus to Ras transformed cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 6:30 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Application/Control Number: 10/563,728

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/Brian Whiteman/

Primary Examiner, Art Unit 1635

Notice of References Cited	Application/Control No. 10/563,728	Applicant(s)/Patent Under Reexamination JACOBS ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-2002/0028195	03-2002	Coffey et al.	424/93.21
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Lee et al. Virology 199, 491-496, 1994
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/22165

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01N 63/00; A61K 48/00

US CL : 424/93.2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/93.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE et al. The interferon-induced double stranded RNA-activated protein kinase induces apoptosis Virology 1994, Vol 199, pages 491-496.	1, 4-6, 8, 11-15
X	US 2002/0155529 A1 (JACOBS et al) 24 October 2002, (24.10.2002), see whole document, especially pages 2-3.	1, 4-8, 11-16
X	US 2003/00444384 A1 (ROBERTS et al) 06 March 2003 (06.03.2003), see whole document, especially pages 11 and 26-28.	1, 3-16

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"B" earlier application or patent published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

09 December 2004 (09.12.2004)

Date of mailing of the international search report

13 JAN 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Brian Whiteman

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/22165

Continuation of B. FIELDS SEARCHED Item 3:

WEST, STN

search terms: vaccinia virus, mutant, oncolytic, E3L, K3L, PKR, inactivation, cancer, tumor, neoplasm



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Date

24.07.06

Reference AM 5279-01EP	Application No./Patent No. 04777944.2 - 2103 PCT/US2004022165
Applicant/Proprietor ARIZONA BOARD OF REGENTS	

COMMUNICATION

The European Patent Office herewith transmits as an enclosure the supplementary European search report under Article 157(2)(a) EPC for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

- ☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

Refund of the search fee

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





European Patent
Office

**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**

Application Number

which under Rule 45 of the European Patent Convention EP 04 77 7944
shall be considered, for the purposes of subsequent
proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 01/35970 A (ONCOLYTICS BIOTECH INC; COFFEY, MATTHEW, C; THOMPSON, BRADLEY, G) 25 May 2001 (2001-05-25) * page 7, line 3 - line 13 * * page 13, line 4 - page 14, line 2 * * page 8, line 14 - line 22 * * page 24, line 28 - page 27, line 23 * -----	1-16	INV. A01N63/00 A61K48/00
X	WO 00/62735 A (PRO-VIRUS, INC; ROBERTS, MICHAEL, S; LORENCE, ROBERT, M; GROENE, WILLI) 26 October 2000 (2000-10-26) * page 7, line 14 - line 18 * * page 22, line 4 - line 22 * * tables 1,2 * * page 40, line 21 - page 41, line 2 * ----- -/--	1-16	
			TECHNICAL FIELDS SEARCHED (IPC)
			A01N A61K
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
INCOMPLETE SEARCH			
The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims: Claims searched completely : Claims searched incompletely : Claims not searched : Reason for the limitation of the search: see sheet C			
Place of search Munich		Date of completion of the search 4 July 2006	Examiner Mauhin, V
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

2
EPO FORM 1503 03.02 (P04C20)



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	SHORS T ET AL: "Complementation of Vaccinia Virus Deleted of the E3L Gene by Mutants of E3L" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 239, no. 2, 22 December 1997 (1997-12-22), pages 269-276, XP004452367 ISSN: 0042-6822 * the whole document *	1	
P,X	WO 2004/003562 A (ONCOLYTICS BIOTECH, INC; THOMPSON, BRADLEY, G; COFFEY, MATTHEW, C) 8 January 2004 (2004-01-08) * the whole document *	1	
			TECHNICAL FIELDS SEARCHED (IPC)



European Patent
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**INCOMPLETE SEARCH
SHEET C**

Application Number
EP 04 77 7944

Although claims 1-10 are directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 04 77 7944

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

04-07-2006

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0135970 A	25-05-2001	AU 782020 B2	30-06-2005
		AU 1262601 A	30-05-2001
		BR 0015491 A	15-10-2002
		CA 2388807 A1	25-05-2001
		EP 1227828 A1	07-08-2002
		JP 2003514024 T	15-04-2003
		MX PA02004736 A	28-01-2003
		NZ 518454 A	30-07-2004
		ZA 200203041 A	09-12-2003
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WO 2004003562 A	08-01-2004	AU 2003245760 A1	19-01-2004
		BR 0311983 A	26-04-2005
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		CN 1666105 A	07-09-2005
		EP 1520175 A2	06-04-2005
		JP 2005531306 T	20-10-2005
		MX PA04012414 A	19-04-2005



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(substantive examination)

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(Formalities and other matters)



Application No. 04 777 944.2 - 2401	Ref. AM 5279-01EP	Date 16.02.2007
Applicant ARIZONA BOARD OF REGENTS		

Communication pursuant to Article 96(2) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 36(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).



Mauhin, Viviane
Primary Examiner
for the Examining Division

Enclosure(s): 3 page/s reasons (Form 2906)

**Bescheld/Protokoll (Anlage)**

Datum
Date 16.02.2007
Date

Communication/Minutes (Annex)

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Sheet 1
Feuille

Notification/Procès-verbal (Annexe)

Anmelde-Nr.:
Application No.: 04 777 944.2
Demande n°:

The examination is being carried out on the **following application documents**:

Description, Pages

1-12 as published

Claims, Numbers

1-16 as published

Drawings, Sheets

1/19-19/19 as published

Reference is made to the following document/s; the numbering will be adhered to in the rest of the procedure:

- D1: WO 01/35970 A (ONCOLYTICS BIOTECH INC; COFFEY, MATTHEW, C; THOMPSON, BRADLEY, G) 25 May 2001 (2001-05-25)
- D2: WO 00/62735 A (PRO-VIRUS, INC; ROBERTS, MICHAEL, S; LORENCE, ROBERT, M; GROENE, WILLI) 26 October 2000 (2000-10-26)
- D3: SHORS T ET AL: "Complementation of Vaccinia Virus Deleted of the E3L Gene by Mutants of E3L" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 239, no. 2, 22 December 1997 (1997-12-22), pages 269-276, XP004452367 ISSN: 0042-6822
- D4: LEE ET AL.: 'The interferon-induced double stranded RNA-activated protein kinase induces apoptosis' VIROLOGY vol. 199, 1994, pages 491 - 496, XP000615910



Datum
Date 16.02.2007
Date

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Anmelde-Nr.:
Application No.: 04 777 944.2
Demande n°:

1. The present application relates to a method of inducing lysis of proliferative cancer cells by contacting said cells with a vaccinia virus (VV) having an inactivating mutation in an interferon resistance gene, preferably E3L and/or K3L, preferably the whole deletion of E3L. Preferably, the cancer cells are ras-transformed cells, breast cancer cells or prostate cancer cells. The present application also relates to a therapeutic composition comprising said vaccinia virus having an inactivating mutation in an interferon resistance gene.
2. Claims 1-10 are directed to methods of treatment. The subject-matter of these claims is not regarded to be susceptible of industrial application. Hence, claims 1-10 should be reformulated (see Article 52(4) and 54(5) EPC and the Guidelines C-IV, 4.2).
3. Notwithstanding the objection in §2 above, it appears that claims 1-16 are not novel over D1 and D2 (Art. 54 EPC).
- 3.1 D1 discloses a method for treating ras-mediated cell proliferative disorder in a mammal, comprising administering to proliferative cells an effective amount of one or more viruses of the group consisting of modified adenovirus, modified HSV, modified vaccinia virus etc, while it results in substantial lysis of the proliferating cells (page 7, lines 3-8). For vaccinia virus, the modified vaccinia virus comprises a mutant gene selected from E3L and K3L (page 7, lines 12-13; page 13, line 4 - page 14, line 2). Pharmaceutical compositions comprising said modified vaccinia virus with a pharmaceutically acceptable carrier are also disclosed (page 8, lines 14-22; page 24, line 28 - page 27, line 23).
- 3.2 D2 discloses a method of treating a neoplasm including cancer in a mammal administering to the mammal a therapeutical amount of an interferon-sensitive, replication-competent vaccinia virus having one or more mutations in one or more viral genes involved with blocking interferon's antiviral activity selected from the group of genes consisting of K3L, E3L and B18R (see page 7, lines 14-18; page 22, lines 4-22; Tables 1 and 2; page 40, line 21 - page 41, line 2).
4. Should the Applicant be able to demonstrate novelty of some or all of the claims, inventive step has to be discussed in view of D1 (or D2) as closest prior art. Indeed,



Bescheld/Protokoll (Anlage)

Communication/Minutes (Annex)

Notification/Procès-verbal (Annexe)

Datum
Date 16.02.2007
Date

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Sheet 3
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Anmelde-Nr.:
Application No.: 04 777 944.2
Demande n°:

there is a strong hint in D1 (and D2) to use a vaccinia virus wherein the E3L and/or K3L gene is not transcribed (see page 13, lines 27-28). The expectation of success is reasonable (in particular in view of D3 or D4) so that there is no surprising effect.

5. It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 29(1) EPC. The applicant should also indicate the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.

HOEFER & PARTNER



HOEFER & PARTNER
Pilgersheimer Straße 20 · D-81543 München/Germany

Europäisches Patentamt

80298 München

EPO - Munich
36

24. Aug. 2007

Ihr Zeichen/your ref

Unser Zeichen/our ref

AM 5279-01EP

PATENTANWÄLTE
EUROPEAN PATENT ATTORNEYS
EUROPEAN TRADEMARK ATTORNEYS
EUROPEAN DESIGN ATTORNEYS

Theodor Hofer – 1992, Dipl.-Ing.
Dr. Horst Schmidt, Dr.-Ing. Dipl.-Ing.
Hans-Werner Schmitz, Dipl.-Ing. Dipl.-Wirtsch.-Ing.
Dr. Joachim Weber, Dr.-Ing. Dipl.-Ing.
Thomas J. Hager, Dipl.-Ing. (FH)
Steffen Schaeberle, Dipl.-Ing.
Ingo Görz, Dipl.-Ing.
Gabriele Leißler-Gerstl, Lbm.-Chem.

RECHTSANWÄLTE
Fachanwälte für gewerblichen Rechtsschutz
Dr. Ulrich Hocke, Dr. jur. Dipl.-Kfm.
Bettina Görz
Oliver Splies

In Kooperation mit
PATENTANWÄLTE
DURM & PARTNER Karlsruhe

Datum/date

23.08.2007

Applicant: Arizona Board of Regents
Serial Number: 04 777 944.2-2103

This is in response to the communication pursuant to Article 96 (2) EPC of 16 February 2007.

Please find enclosed a new set of claims substituting the claims as presently on file. The claims have been amended to overcome the objections raised in the office action. First of all the claims have been reworded a second medical use claims. Moreover, the claims are now related to the use of vaccinia virus mutants having a truncated E3L gene that replicates in breast cancer cells but not in normal breast cells for preparing a medicament for inducing lysis of proliferating cancer cells.

The disclosure for a new claim 1 is found on page 4, lines 6 to 11, and Fig. 1 of the description.

It has been found by the inventors of the present application that a vaccinia virus having a truncation and particularly a truncation of less than 83 amino acids from the amino terminus and being able to replication in human breast cancer cells but not in normal breast cells has a selective oncolytic activity for cancer cells. It has been found that vaccinia virus is highly resistant to treatment of cells with interferon. The inventors found that vaccinia virus having E3L completely deleted has a high ras dependency but cannot inhibit PKR. On the other hand a vaccinia mutant Δ 83N is toxic and induces morbidity. However, if a vaccinia virus mutant is used having a truncation, particularly a truncation at the amino terminus of E3L which is less than 83 amino acids, and which can replicate in human breast cancer cells but not in normal breast cells, this vaccinia virus can be used to induce lysis of proliferating cancer cells. As can be seen from Fig. 1, mutants having a truncation at the amino terminus or the

carboxy terminus but having a truncation of less than 83 amino acids on the amino terminus have the optimal combination of PKR inhibition and high ras dependency.

The mutants as now claimed, wherein the E3L gene is truncated, are not transcribed and do not replicate in breast cells, which is critical for the oncolytic activity. The description provides a test to access if a mutant selectively replicates in breast cancer cells but not normal breast cells. This test is outlined on page 9, lines 16 to 22. Viral replication is measured by determining how many infectious virus particles are present after 72 hours of culturing. Thus, those vaccinia virus mutants that are useful for the present invention can be found by the skilled artisan using routine experiments.

The documents cited by the Examiner neither anticipate nor render obvious the subject matter of the present invention. WO 01/35970 (D1) teaches viruses for the treatment of cellular proliferative disorders and uses modified viruses, inter alia modified vaccinia virus having a mutant gene selected from the group consisting of E3L and K3L. There is no indication as to the mutation but only the hint to delete or disrupt the E3L gene. WO 00/62735 (D2) is even more general and teaches that a vaccinia virus having one or more mutations in one or more viral genes selected from K3L, E3L and B18R can be used to treat neoplasm. However, also D2 does not give any guidance to the site or type of mutation that could result in a vaccinia virus having selective oncolytic activity. The inventors surprisingly found that the full deletion of E3L results in the failure of the vaccinia virus to replicate in normal or cancerous breast cells and that treatment of breast cancer xenografts with E3L Δ 83N mutant vaccinia virus results in toxicity and morbidity. If however vaccinia virus has a truncation of less than 83 amino acids and replicates in human breast cancer cells but not normal breast cells it induces selectively and effectively oncolytic regression of breast cancer xenografts.

Thus, the subject matter of the claims as now valid is novel and inventive with regard to D1 and D2.

It is assumed that the Examiner can now accept patentability of the present application. If there are further deficiencies a telephone call or the appointment of a personal interview would be highly appreciated. Otherwise it is requested to summon to oral proceedings in accordance to Article 116 EPC.



Gabriele Leißler-Gerstl
European Patent Attorney

Encl.
New Set of Claims

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

To:

BUTTER, Gary, M
Baker Botts LLP
30 Rockefeller Plaza
New York, NY 10112-4498
NY 10112
ETATS-UNIS D'AMERIQUE

BAKER BOTTS LLP
RECEIVED

FEB 06 2006

Date of mailing (day/month/year)

19 January 2006 (19.01.2006)

Applicant's or agent's file reference

35892-PCT

- 072448.0374

IMPORTANT NOTICE

International application No.

PCT/US2004/022165

International filing date (day/month/year)

08 July 2004 (08.07.2004)

Priority date (day/month/year)

08 July 2003 (08.07.2003)

Applicant

ARIZONA BOARD OF REGENTS et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Dorothee Mülhausen

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 35892-PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2004/022165	International filing date (day/month/year) 08 July 2004 (08.07.2004)	Priority date (day/month/year) 08 July 2003 (08.07.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant ARIZONA BOARD OF REGENTS			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | |
|---|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report |
| <input type="checkbox"/> Box No. II | Priority |
| <input type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Date of issuance of this report 09 January 2006 (09.01.2006)
	Authorized officer Dorothee Mülhausen Telephone No. +41 22 338 87 40

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 17 JAN 2005

PCT MPO PCT

To:
GARY M. BUTTER
BAKER BOTTS L.L.P.
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112-4498

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 35892-PCT		Date of mailing (day/month/year) 13 JAN 2005
FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/US04/22165	International filing date (day/month/year) 08 July 2004 (08.07.2004)	Priority date (day/month/year) 08 July 2003 (08.07.2003)
International Patent Classification (IPC) or both national classification and IPC IPC(7): A01N 63/00; A61K 48/00 and US Cl.: 424/93.2		
Applicant ARIZONA BOARD OF REGENTS		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US
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Authorized officer
Brian Whiteman

Telephone No. (703) 308-0196

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/22165

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☐ in written format
☐ in computer readable form

c. time of filing/furnishing

- ☐ contained in international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/22165

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>2</u>	YES
	Claims <u>1, 3-16</u>	NO
Inventive step (IS)	Claims <u>2</u>	YES
	Claims <u>1, 3-16</u>	NO
Industrial applicability (IA)	Claims <u>1-16</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1 and 3-16 lack novelty under PCT Article 33(2) as being anticipated by ROBERTS et al. ROBERTS teaches a method of treating a tumor comprising contacting the tumor with an interferon sensitive vaccinia virus having one or more mutations selected from the group consisting of K3L, E3L and B18R. ROBERTS teaches that the tumor can be a prostate or breast tumor. ROBERTS further teaches that the tumor can be in a mammal and the vaccinia virus can be administered intravenously to the tumor in the mammal.

Claims 1 and 3-16 lack an inventive step under PCT Article 33(3) as being obvious over ROBERTS et al. ROBERTS teaches a method of treating a tumor comprising contacting the tumor with an interferon sensitive vaccinia virus having one or more mutations selected from the group consisting of K3L, E3L and B18R. ROBERTS teaches that the tumor can be a prostate or breast tumor. ROBERTS further teaches that the tumor can be in a mammal and the vaccinia virus can be administered intravenously to the tumor in the mammal.

Claim 2 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest treating cancer cells that are ras-transformed with a vaccinia virus having an inactivation mutation in an interferon resistance gene.

Claims 1-16 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry for inducing lysis of proliferating cancer cells.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/22165

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01N 63/00; A61K 48/00

US CL : 424/93.2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/93.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE et al. The interferon-induced double stranded RNA-activated protein kinase induces apoptosis Virology 1994, Vol 199, pages 491-496.	1, 4-6, 8, 11-15
X	US 2002/0155529 A1 (JACOBS et al) 24 October 2002, (24.10.2002), see whole document, especially pages 2-3.	1, 4-8, 11-16
X	US 2003/00444384 A1 (ROBERTS et al) 06 March 2003 (06.03.2003), see whole document, especially pages 11 and 26-28.	1, 3-16

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

09 December 2004 (09.12.2004)

Date of mailing of the international search report

13 JAN 2005

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Date

29.12.06

Reference
EPA-94 857

Application No./Patent No.
03765541.2 - 1223 PCT/US0321764

Applicant/Proprietor
ARIZONA BOARD OF REGENTS

COMMUNICATION

The European Patent Office herewith transmits as an enclosure the supplementary European search report under Article 157(2)(a) EPC for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

- ☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

Refund of the search fee

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	XIANG YING ET AL: "Blockade of interferon induction and action by the E3L double-stranded RNA binding proteins of vaccinia virus" JOURNAL OF VIROLOGY, vol. 76, no. 10, May 2002 (2002-05), pages 5251-5259, XP002410981 ISSN: 0022-538X * the whole document *		INV. C07K14/065 C07K14/07 C12N15/863
A	& XIANG YING ET AL: "Vaccinia virus E3L suppresses the IFN system by preventing activation of antiviral enzymes and IRF3 phosphorylation" JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, vol. 24, no. Supplement 1, 2001, pages S.70-S.71, XP008072611 & ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR INTERFERON AND CYTOKINE RESEARCH; CLEVELAND,, OH, USA; OCTOBER 07-11, 2001 ISSN: 1079-9907 * abstract *		TECHNICAL FIELDS SEARCHED (IPC)
A	----- BRANDT T A ET AL: "BOTH CARBOXY- AND AMINO-TERMINAL DOMAINS OF THE VACCINIA VIRUS INTERFERON RESISTANCE GENE, E3L, ARE REQUIRED FOR PATHOGENESIS IN A MOUSE MODEL" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 75, no. 2, January 2001 (2001-01), pages 850-856, XP002951113 ISSN: 0022-538X * the whole document * ----- -/--		C07K C12N
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search The Hague		Date of completion of the search 11 December 2006	Examiner Schulz, Regine
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	

1
EPO FORM 1503 03.82 (P04C04)



European Patent
Office

**SUPPLEMENTARY
EUROPEAN SEARCH REPORT**

Application Number
EP 03 76 5541

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
P,X	VIJAYSRI S ET AL: "The Orf virus E3L homologue is able to complement deletion of the vaccinia virus E3L gene in vitro but not in vivo" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 314, no. 1, 15 September 2003 (2003-09-15), pages 305-314, XP004457949 ISSN: 0042-6822 * the whole document *	1-11	
T	LANGLAND ET AL: "Inhibition of PKR by RNA and DNA viruses" VIRUS RESEARCH, AMSTERDAM, NL, vol. 119, no. 1, July 2006 (2006-07), pages 100-110, XP005455777 ISSN: 0168-1702 * the whole document *		
			TECHNICAL FIELDS SEARCHED (IPC)
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search The Hague		Date of completion of the search 11 December 2006	Examiner Schulz, Regine
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

1
EPO FORM 1503 03.02 (P04004)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/21764

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 39/285; C12N 15/863 US CL : 424/232.1, 199.1; 435/320.1, 69.1, 235.1 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/232.1, 199.1; 435/320.1, 69.1, 235.1 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,372,455 B1 (JACOBS et al) 16 April 2002, see entire document.	1-11
X	WO99/55910 A1 (ARIZONA BOARD OF REGENTS) 04 November 1999, see page 3 line 27 - page 5 line 17, claims 8, 14, 20.	2, 4, 5
Y	WO 92/12240 A1 (VIROGENETICS CORPORATION) 23 July 1992, see claims 1, 2, 9, 10.	2-9
Y	BEATTIE et al. Reversal of the interferon-sensitive phenotype of a vaccinia virus lacking E3L by expression of the reovirus S4 gene. Journal of virology. Jan 1995, vol. 69, no. 1, pages 499-505.	2-9
A	ROSENTHAL et al. Developing new smallpox vaccines. Emerging Infectious Diseases. November-December 2001. Vol. 7, no. 6, pages 920-926.	1, 10, 11
A	M.E. In search of a kinder, gentler vaccine. Science. 31 May 2002. Vol. 296, page 1594.	1, 10, 11
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 12 November 2003 (12.11.2003)		Date of mailing of the international search report 14 APR 2004
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer Mary E. Mosher, Ph.D. Telephone No. 703-308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/21764

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 12-14
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 12-14 require search of SEQ ID NO:1, and no sequence listing was provided.
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/21764

Continuation of B. FIELDS SEARCHED Item 3:

EAST USPAT, PGPUB, EPO, JPO, DERWENT; Medline. Search terms: E3L, vaccinia, delet?, vp1080, interferon sensitiv\$, pox, poxivr\$, paoletti, perkus, tartaglia, jacobs.